UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/893,737	06/28/2001	Paul O. Sheppard	00-41	3361

7590 05/27/2003

Robyn Adams
ZymoGenetics, Inc.
1201 Eastlake Avenue East
Seattle, WA 98102

EXAMINER
SMITH, CAROLYN L

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 05/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/893,737	SHEPPARD ET AL.	
	Examiner	Art Unit	
	Carolyn L Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-9 and 12-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-9 and 12-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: Sequence Match Listing (1 page).

DETAILED ACTION

Applicants' election of Group II (claims 7-9 and 12-14) and SEQ ID NO: 1, cancellation of claims 1-6, 10-11, and 15-19; amendment of claims 7, 8, 12, and 13 in Paper No. 7, filed 3/11/03, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The present title is directed to mammalian secreted proteins, whereas in contrast the elected claim is specifically directed to polynucleotides, expression vectors, and cultured cells.

Claims herein under examination are 7 (amended), 8 (amended), 9, 12 (amended), 13 (amended), and 14.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, such as on page 49, line 18. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

PATENTABLE UTILITY GUIDELINES

The pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph, "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.

The examiner is using the following definitions in evaluating the claims for utility.

"Specific" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

Claims Rejected Under 35 U.S.C. § 101

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 7-9 and 12-14 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility.

The critical limitations of claims 7-9 and 12-14 is the nucleotide sequence of the claimed nucleic acids, expression vectors, and cells, SEQ ID NO: 1. The claimed nucleic acids, expression vectors, and cells are not supported by a specific utility, because the disclosed uses of these compositions are not specific and are generally applicable to many polynucleotides encoding secretory proteins. The specification states a secretory peptide of a protein encoded by the claimed polynucleotides can be used to direct the secretion of other proteins (page 10, lines 3-4), fusion proteins can be created to produce multimeric analogs (page 12, lines 6-10), and the

proteins can be used for diagnostic and therapeutic purposes (page 12, lines 14-15). The specification states the polynucleotides can be used for screening (page 16, lines 11-12), making probes/primers (page 22, lines 1-2), and assessing genetic expression (page 22, lines 35-36). The specification states the claimed cells can be used in a drug selection process (page 24, lines 35-37). The specification summarizes general sequence uses in modern biotechnology, but never connects the specifically elected sequence (SEQ ID NO: 1) to any particular or available utility. The above-mentioned list of possible utility for the claimed sequence falls short of a readily available utility. These are non-specific uses that are applicable to many nucleic acids, expression vectors, and cells, and are not particular or specific to the nucleic acid, expression vector, and cell being claimed.

Further, these claimed nucleic acids, expression vectors, and cells are not supported by a substantial utility, because no substantial utility has been established for the claimed subject matter. SEQ ID NO: 1 may indeed be the sequence that encodes a secretory protein; however, further research would be required to confirm a "real world" context of use. For example, the specification notes that sequence analysis "predicts" that the encoded protein includes an amino-terminal secretory peptide (page 7, lines 8-9 and Table 1). However, they do not provide data to confirm that the polynucleotide, particularly SEQ ID NO: 1, actually encodes a secretory protein or how this information can be used outside of a research laboratory and in the "real world". Further research testing of sequence of SEQ ID NO: 1 is needed to see if it encodes a secretory protein and whether this plays a crucial role in a substantial utility, or alternatively, if its presence is inconsequential. Identifying a sequence itself does not define a "real world" context of use.

Applicant should explicitly identify a specific, substantial, and credible utility for the claimed invention and establish a probative relation between any evidence of record and the originally disclosed properties of the claimed invention.

Due to a lack of either an art recognized or alleged well established utility, the instant invention has been rejected due to also lacking the required combination of a specific, substantial, and credible utility. Although it may be credible that the polynucleotide of SEQ ID NO: 1 encodes a secretory protein, the lack of a specific and substantial utility, as explained above, sufficiently supports this rejection.

It is noted applicants have stated in the specification that sequence analysis predicts that the protein encoded by the polynucleotide includes an amino-terminal secretory peptide (page 7, lines 8-9). Absent factual evidence, one skilled in the art would have reason to doubt that sequence similarity alone would reasonably support the assertion that the biological activity of the claimed subject matter would be the same as that of the similar sequence. Furthermore, it is unclear whether the similar sequence identified in the prior art has actually been tested for the biological activity or whether this also is an asserted biological activity based upon sequence similarity to yet a different sequence. Note that it would have been well known in the art that sequence similarity does not reliably correlate to structural similarity and that structural similarity does not reliably result in similar or identical biological activities. For example, it would have been well known that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. In the absence of factual evidence characterizing the structural and functional components of the biomolecule, the effects of these changes are largely unpredictable as to which ones will have a significant

effect and which ones will be silent mutations having no effect. Several publications document the unpredictability of the relationship between sequence, structure, and function, although it is acknowledged that certain specific sequences have been found to be conserved in biomolecules having related function following a significant amount of further research. See Lopez et al. (Molecular Biology, 32:881-891,1999); Attwood (Science, 290:471-473, 2000); Gerhold et al. (BioEssays, 18(12):973-981, 1996); Wells et al. (Journal of Leukocyte Biology, 61(5):545-550, 1997); and Russell et al. (Journal of Molecular Biology, 244:332-350, 1994). However, this level of factual evidence is absent here.

Claim Rejections – 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of the skill in molecular

biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

LACK OF ENABLEMENT

Claims 7-9 and 12-14 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the claimed invention.

For a sequence putatively assigned a biological function, even if correct, does not appear to be defined as to what use it is to be applied. The significance of the sequence is unconfirmed, further rendering it indiscernible how someone of skill in the art would use such an entity.

Due to the large quantity of experimentation necessary to determine activity or property of the disclosed nucleic acid, expression vector, and cell, such that it can be determined how to use the claimed sequence, the lack of direction/guidance presented in the specification regarding the same, and the absence of working examples directed to the same, the specification fails to teach the skilled artisan how to use the claimed invention.

Also, since the claimed invention is not supported by a specific, substantial, and credible utility or a well-established utility for the reasons set forth above (refer to the 35 U.S.C. § 101 rejection), one skilled in the art would not know how to use the claimed invention.

LACK OF WRITTEN DESCRIPTION

Claims 7-9 and 12-14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time of the invention was filed, had possession of the claimed invention.

The specification discloses SEQ ID NO: 1 and 2 which corresponds to nucleic acid sequence the encoded polypeptide. SEQ ID NO: 1, its full complement, and SEQ ID NO: 2 meet the written description provisions of 35 U.S.C. 112, first paragraph. Due to the open claim wording of "comprising" in claims 7-9 and 12-14, these claims are directed to encompass polynucleotide and polypeptide sequences that do not meet the written description provision of 35 U.S.C. 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by these claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 1 and 2, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only SEQ ID NO: 1, its full length complement, and SEQ ID NO: 2, but not the full breadth of the claims, meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Claims Rejected Under 35 U.S.C. § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claim 7 recites the phrase "comprising *the* sequence of nucleotides" which is vague and indefinite. It is unclear if the nucleic acid molecule is referring to the entire nucleotide sequence

of SEQ ID NO: 1 or just a fragment of the sequence. Clarification of the metes and bounds of the claim via clearer claim wording is requested.

Claim 13 (line 4) recites the phrase "according to" which is vague and indefinite. It is unclear to what extent claim 12 must be followed. Clarification of the metes and bounds of the claim via clearer claim wording is requested.

Claim Rejections – 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 7 is rejected under 35 U.S.C. 102(a) as being anticipated by Briggs et al. (P/N 6,068,976).

Due to the fact that claim 7 contains open claim language "comprising" which can include polynucleotide fragments, Briggs et al. disclose a polynucleotide of SEQ ID NO: 4 containing a fragment (residues 1075-1092) which identical to a fragment (residues 317-334) of SEQ ID NO: 1 of the instant invention (see Sequence Match Listing). Thus, Briggs et al. anticipate the limitations in claim 7.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (703) 308-6043. The examiner can normally be reached Monday through Friday from 8 A.M. to 4:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

May 20, 2003

ARDIN H. MARSCHEL
PRIMARY EXAMINER